



Figure S3. Control experiments for cell depletion *in vivo*, serum antibodies and phagocytosis in BALB/c mice. BALB/c mice were infected by the i.v. route with a mixture of four different strains of *S. pneumoniae*: TIGR4 (green), D39 (filled red circles), DP1004 (open red circles) and G54 (blue) at the challenge dose of 2.5×10^5 CFU/each strain (total 1×10^6 CFU/mouse). Bacterial blood counts at different time point are reported for infected mice treated with clodronate liposomes (A), PBS liposomes (B), anti-GR1 mAb (E), isotype control rat IgG2b,k (F) and untreated mice (C and G). Data are represented as the mean \pm SD of blood bacterial counts of three mice. Macrophage depletion (D) and neutrophil depletion (H) were confirmed by flow cytometry analysis with specific antibodies: anti-F4/80 and anti-CD11b for macrophage in the spleen and liver (D) and anti-GR-1 for neutrophil (H). Mean \pm SD of triplicate of independent experiments are shown. (I) Growth of D39 (red), TIGR4 (green) and G54 (blue) pneumococcal strains in rotated fresh blood from BALB/c mice. A representative experiments is reported. (J) Effect of anti-capsular serotype 2 serum (1:100) to survival of 3×10^5 CFU/ml of D39 (red bar) and its non-encapsulated derivative DP1004 (open bar) in mouse blood incubated for 1 h. Mean \pm SD of three independent experiments are reported and statistical analysis is performed by Student's *t*-test. (K) Binding of anti-type 2 specific antibody (1:100) to whole pneumococci TIGR4 (green bar), D39 (red bar), G54 (blue bar) and rough DP1004

(red open bar) after 1 h incubation at 37°C. No binding was observed with non-immunized serum (1:100) from naïve BALB/c mice. Data are represented as FI \pm SEM of three independent experiments.